REMARKS

Claims 1-39 and 69 remain before the Examiner for reconsideration. Claims 13, 14, 17, 40-68 and 70-103 have been withdrawn.

In accordance with Section 713.04 of the Manual of Patent Examining Procedure (MPEP) and 37 CFR §1.133(b), a Statement of the Substance of the Interview between Examiner James W. Rogers and Mr. Henry Bartony is enclosed with this amendment.

Applicants respectfully request that said Statement of the Substance of the Interview be made of record in the Patent and Trademark office.

In the Office Action dated September 21, 2006 the Examiner indicated that Applicants election with traverse of invention I in the reply to the Restriction Requirement filed August 15, 2006 has been acknowledged. With respect to the transversal, the Examiner indicated that:

> The traversal is on the ground(s) that inventions I and IV should be combined. This is found persuasive because a search for groups I and IV will require search of essentially the same art and will not put an undue burden on the examiner. Thus group IV has been combined with group I.
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> The requirement for restriction between group I and groups II-III,V-IX is still deemed proper and is therefore made FINAL.

Applicants respectfully acknowledge the combination of group IV with group I.

The Examiner also rejected Claims 1, 10-12, 19-22, 27, 34-35 and 69 are rejected under 35 U.S.C. 102(b) "as being anticipated by Liptova et al. (Macromol. Symp. 152, 139-150 (2000), cited by applicant)." Specifically, the Examiner asserted that:

> Liptova teaches hemocompatable (same as biocompatible) and biodegradable polyurethanes containing bioactive heparine fragments, which are prepared from diisocyanates, oligoetherglycols, chain extenders and heparin, which comprises a plurality of hydroxyl groups and has a therapeutic effect in the body. See pag 145-148 2nd paragraph. The biocompatible and biodegradable polyurethanes containing bioactive heparine fragments were used for the creation of artificial blood vessels.

Applicants respectfully traverse the Examiner's rejection.

To assert anticipation under Section 102(b) the cases hold that the Examiner:

> must show that each element of the claim in issue is found, either expressly described or under principles on inherency, in a single prior art reference, or, that the claimed invention was previously known or embodied in a single prior art device or practice.

Kalman v. Kimberly-Clark Corp., 713 F.2d 760, 771, 218 USPQ 781, 789 (Fed. Cir. 1983), cert. Denied, 465 U.S. 1026 (1984); Tyler Refrigeration v. Kysor Industrial Corp., 777 F.2d 687, 689, 227 USPQ 845, 846-47 (Fed. Cir. 1984) (judgment of anticipation reversed). "In deciding the issue of anticipation, the trier of fact must identify the elements of the claims, determine their meaning in the light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference." Lindemann, 730 F.2d at 1458, 221 USPQ at 485; Kalman, 713 F.2d at 771, 218 USPQ at 789.

"The test for determining if a reference anticipates a claim of a patent is whether the reference contains within its four corners adequate directions for the practice of the patent claim ... ." Kistler Instrument A.G. v. United States, 628 F.2d 1303, 1311, 203 USPQ 511, 519, aff'd., 211 USPQ 920 (Ct. Cl. 1980). The reference, whether foreign or domestic, patent or otherwise, must be construed strictly for what it "clearly and definitely discloses." Application of Boling, 292 F.2d 306, 310-11, 130 USPQ 161, 164 (CCPA 1961); Aluminum Co. of Am. v. Sperry Products, Inc., 285 F.2d 911, 922, 127 USPQ 394, 403 (6th Cir. 1960), cert. denied, 368 U.S. 890 (1961). A patent is not anticipated by a reference "unless the latter exhibits the invention in such full, clear and exact terms as to enable any person skilled in the art to practice it without making experiments." 285 F.2d at 922, 127 USPQ at 403.

Under the appropriate standard as set forth above, Liptova does not anticipate the present invention. Liptova discloses that heparin is incorporated within the polymer matrix of the polyurethane polymer thereof. The polyurethane polymer is capable of biodegradation via fragmentation of the polymer. Heparin is incorporated in the polymer to improve hemocompatibility. However, there is no disclosure or suggestion in Liptova that heparin itself is released into the body upon degradation of the polyurethane polymer matrix of Liptova. In that regard, upon degradation of the polymer of Liptova, heparin would be incorporated within degradation fragments, but heparin itself would not be released as a result of the degradation. To

the contrary, the present invention requires the bioactive agent be released as a degradation product.

The Examiner also rejected Claims 1-4,7-8,12,19,22,27-30,33 and 69 under 35 U.S.C. 102(e) "as being anticipated by Woodhouse et al. (US 6,221,997 B1, cited by applicant)." Specifically, the Examiner asserted that:

> Woodhouse teaches biodegradable polyurethane materials synthesized from an amino acid based diisocyanate such as lysine, a polyol and an amino-acid chain extender. See col 2 lin 21-col 3 lin 30, col 6 lin 35-col 7 lin 5 and col 8 lin 20-39. Regarding the limitation of a bioactive agent with at least one reactive group -X, while Woodhouse teaches that the amino acids used are chain extenders, the amino acids within are degradable by enzymes thus meeting the limitation of a bioactive agent. Also the amino acids could have a plurality of reactive amine groups.

Applicants respectfully traverse the Examiner's rejection.

Woodhouse discloses a biodegradable polyurethane formed by reaction of a polyol, a diisocyanate, and a chain extender. The chain extender is the reaction product of a diol with an amino acid that is in such a condition that it can be recognized by a biological agent in the form of an enzyme. In that regard, the amino acid is subject to enzymatic degradation. Amino acid-based or other aliphatic diisocyanates are disclosed as preferred, as the toxicity of the resulting degradation products is less than that of conventional aromatic diisocyanates. Aliphatic diols such as 1,4-cyclohexane dimethanol are disclosed as preferred for the synthesis of the chain extender.

It is indicated that the amino acid is likely a final product of degradation of the ester and urea groups of the chain extender section. Applicants have amended claims 1, 27 and 69 to more clearly indicate that amino acids are not bioactive agents as claimed in the present invention.

The enzymatic degradation of Woodhouse is limited to the particular structure of the polymers thereof- that is specific to the amino acid (for example, phenylalanine) - and to the enzyme that "recognizes" the amino acid group within the polymer. Woodhouse does not disclose or suggest how an entity other than an amino acid such as the bioactive agents of the present invention can be incorporated into the polymer thereof so that the bioactive agent is released as a biodegradation product.

Claims 1-39 and 69 are rejected by the Examiner under 35 U.S.C. 103(a) "as being unpatentable over Zhang et al. (Biomaterials 21 (2000) 1247-1258, cited by applicants)." Specifically, the Examiner asserted that:

> Zhang discloses biodegradable peptide-based urethane polymers synthesized by lysine diisocyanate (LDI) ethyl ester and glycerol (hydroxylated biomolecule) which were further reacted with water as the chain extender, forming foams for tissue engineering applications, the foams supported the growth of rabbit bone marrow stomal cells in vitro. See entire article. Zhang does not disclose in the experimental section a polyurethane embedded with a bioactive agent, however to do so would have been obvious due to the disclosure within that LDI-glycerol polymer may allow incorporation of proteins of interest (cell attachment factors and/or growth factors) to regionally promote a microenvironment optimal for cell organization and stimulation. See page 1248 left col, Vt paragraph. Regarding claim 23 the limitation of pore size is met by Zhang's discloser that the pore size can be 10 pm to 2 mm in diameter. See page 1252, right col. 2nd paragraph. Zhang who disclosed that the free isocyanate content is 1.26% meets claims 24 and 36 limitation on the free isocyante content. See page 1252 right col. 1s paragraph. Regarding claims 25-26 and 37-38 the NCO:OH equivalent limitations are met because Zhang discloses that 55 mmol of glycerol was added to 87 mmol of LDI, since LDI has two reactive sites (NCO) and glycerol has three (OH) the NCO:OH equivalent is 1.05.

Applicants respectfully traverse the Examiner's rejection.

As admitted by the Examiner elsewhere in the Office action "Zhang while disclosing the peptide based urethane polymer may allow incorporation of proteins of interest such as cell attachment and/or growth factors does not give any working examples." Indeed, Zhang does not disclose even what is meant by incorporation of proteins. In that regard, in the present invention an isocyanate group of at least one multifunctional isocyanate compound is reacted with the bioactive agent, thereby covalently bonding the bioactive agent within the polyurethane composition. There is no disclosure or suggestion of the covalent attachment of a protein or any other bioactive group within the polymer of Zhang or how a protein could be covalently incorporated within the polymer matrix of Zhang. The disclosure of Zhang is not enabling for the covalent incorporation of a protein therein. Moreover, a protein can be physically "incorporated" within the polymer matrix of Zhang without covalent attachment of the protein within the polymer via, for example, an encapsulation or entrapment process. Furthermore, there is no disclosure of how or if the polymer of Zhang would degrade to release a protein (or other bioactive agent) as a degradation product should such a protein (or other bioactive agent) be covalently incorporated into the polymer thereof.

The Examiner rejected claims 1-39 and 69 under 35 U.S.C. 103(a) "as being unpatentable over Zhang et al. (Biomaterials 21 (2000) 1247-1258, cited by applicants) in view of Liptova et al. (Macromol. Symp. 152, 139-150 (2000), cited by applicant)." Specifically, the Examiner asserted that:

> Zhang is disclosed above. Zhang while disclosing the peptide based urethane polymer may allow incorporation of proteins of interest such as cell attachment and/or growth factors does not give any working examples.
>
> Liptova is disclosed above. Liptova is used to primarily show that it was already well known in the art at the time of the invention to incorporate bioactive proteins (heparin) into biodegradable polyurethane/polyol polymers.
>
> It would have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to combine the art described in the documents above because Zhang discloses all of applicants claimed invention and even discloses the peptide based urethane polymer may allow incorporation of proteins of interest while Liptova is used to show that incorporating bioactive proteins (heparin) into biodegradable polyurethane/polyol polymers was already known in the art at the time of the invention. The motivation to combine the above documents would be to synthesize a biodegradable polyurethane containing a bioactive protein that may be applied as a prosthetic appliance in direct contact with living tissues. Thus, the claimed invention, taken as a whole was prima facie obvious over the combined teachings of the prior art.

Applicants respectfully traverse the Examiner's rejection.

Liptova does not overcome the deficiencies of Zhang as set forth above. Once again, Zhang is not enabling for the covalent incorporation therein of a protein or other bioactive agent of the present invention. Moreover, even if a bioactive agent were covalently incorporated it is not clear how such incorporation would be effected to provide the bioactive agent as a degradation product. Moreover, as set forth above, heparin is not released upon degradation of the polymer of Liptova. Furthermore, heparin is not a protein, but a glycosaminoglycan.

In view of the above amendments and remarks, Applicants respectfully requests that the Examiner, indicate the allowability of the Claims, and arrange for an official Notice of Allowance to be issued in due course.

Respectfully submitted,
ERIC J. BECKMAN et al.

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By /Henry E. Bartony, Jr., Reg. No. 34,772/
Henry E. Bartony, Jr., Esq.
Reg. No. 34,772

Bartony & Hare, LLP
Suite 1801, Law & Finance Building
429 Fourth Avenue
Pittsburgh, Pennsylvania 15219
412-338-8632 (telephone)
412-338-6611 (fax)

Attorney for Applicant